



# Hashimoto Encephalopathy

## Haşimato Ensefalopatisi

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Hashimoto encephalopathy (HE) is a steroid-responsive, acute or subacute encephalopathy, characterised by autoimmune thyroiditis associated with elevated antithyroid antibody titres. An 11-year-old girl was admitted to the Department of Paediatrics with generalised tonic-clonic seizures, left facial paralysis and right hemiparesis. Ceftriaxone and acyclovir were applied, and methyl prednisolone 2 mg kg<sup>-1</sup> day<sup>-1</sup> was administered orally. The hemiparesis improved on the 3<sup>rd</sup> day of treatment, but the facial paralysis persisted into the 15<sup>th</sup> day. When she developed somnolence, she was transferred to the paediatric intensive care unit and provided with respiratory support after intubation. Antithyroid peroxidase (Anti-TPO) and Antithyroglobulin antibody (Anti-Tg) levels were measured at 112.3 IU mL<sup>-1</sup> and 74.6 IU mL<sup>-1</sup>, respectively. HE was considered as the provisional diagnosis, for which intravenous methyl prednisolone 30 mg kg<sup>-1</sup> for 5 days followed by prednisolone 1.5 mg kg<sup>-1</sup> day<sup>-1</sup> were administered. The patient's clinical status did not improve; therefore, she underwent therapeutic plasma exchange (1/1 ratio) for 8 days, followed by intravenous immunoglobulin 1 gr kg<sup>-1</sup> for 2 days. As her clinical condition did not improve, rituximab and endoxane treatments were planned. Unfortunately, these treatments were postponed as she developed ventilator-associated pneumonia at the follow-up. She developed septic shock on the 14th day of follow-up, and noradrenaline and dopamine infusions were commenced. Despite all the efforts, she remained unresponsive and died from cardiac arrest. By reporting this case, we aimed to stress that HE should be considered as an aetiology of encephalopathy when infectious, neoplastic, autoimmune, toxic and metabolic causes are excluded.

**Keywords:** Hashimoto encephalopathy, thyroid autoantibodies, children

Haşimato ensefalopatisi, antitiroid antikörlerin yüksekliği ile ilişkili otoimmün tirodit ile karakterize, steroide yanıtı akut ya da subakut ensefalopatidir. On bir yaşında kız hasta, ani gelişen jeneralize tonik klonik nöbet, sol fasial paralizi ve sağ hemiparezi nedeniyle pediatri servisine yatırıldı. Seftriakson ve asiklovir tedavileri başlandı. Metil prednizolon 2 mg kg<sup>-1</sup> peroral verildi. Tedavinin 3. gününde sağ hemiparezi düzeldi, 15. gününde fasyal paralizisi devam eden hastanın uykuya meyilli olduğu gözlemlendi, kliniği saatler içerisinde bozuldu. Hasta çocuk yoğun bakım ünitesine transfer edildi, entübe edilerek mekanik ventilatör ile solunum desteği verildi. Anti tiroidperoksidaz (anti-TPO): 112,3 IU mL<sup>-1</sup>, Antitiroglobülin (Anti-Tg): 74,6 IU mL<sup>-1</sup> saptandı. Bu bulgularla hastada Haşimato ensefalopatisi düşünüldü, 30 mg kg<sup>-1</sup> metil prednizolon tedavisi başlandı ve 5 gün uygulandı, ardından 1,5 mg kg<sup>-1</sup> gün<sup>-1</sup> prednizolon tedavisine geçildi. Kliniğinde düzelme gözlenmeyen hastaya 8 gün terapotik plazma değişimi (1/1 oranında) yapıldı ardından 2 gün 1 gr kg<sup>-1</sup> intravenöz immünglobülin (IVIG) verildi. Kliniğinde düzelme gözlenmedi, Rituksimab ve endoksan tedavilerinin verilmesi planlandı. Ancak izleminde ventilatör ilişkili pnömoni gelişti, Rituksimab ve endoksan tedavileri ertelendi. İzleminin 14. gününde septik şok gelişen hastada noradrenalin ve dopamin infüzyonuna başlandı, ardiak arrest gelişen hasta kaybedildi. Bu olgu ile ensefalopati etiyolojisi araştırılırken enfeksiyon, tümör, otoimmün, toksik ve metabolik nedenlerin saptanamadığı durumlarda Haşimato ensefalopatisinin hatırlanması gerektiğini vurgulamak istedik.

**Anahtar Kelimeler:** Haşimato ensefalopatisi, tiroid otoantikörleri, çocuk

## Introduction

Hashimoto encephalopathy (HE) is a steroid-responsive, acute or subacute encephalopathy, characterised by autoimmune thyroiditis associated with elevated levels of antithyroid antibodies (1). Its prevalence is 2.1/100.000; however, it is uncommon in the paediatric population, with merely 60 cases having been reported so far (2). The role of antibodies in the aetiology of the condition is unclear, and there is no correlation between antibody titres and symptom severity (3).

## Case Presentation

An 11-year-old girl was admitted to the Department of Paediatrics with sudden-onset generalised tonic-clonic seizures, left facial paralysis and right hemiparesis. Her past history was not remarkable, and her immunisation schedule was complete. On physical examination, she had left central facial paralysis and her deep tendon reflexes were hyperactive. Other systems were normal. Her haemoglobin level was 11.6 g dL<sup>-1</sup>, white blood cell count 16.3 µL<sup>-1</sup>,

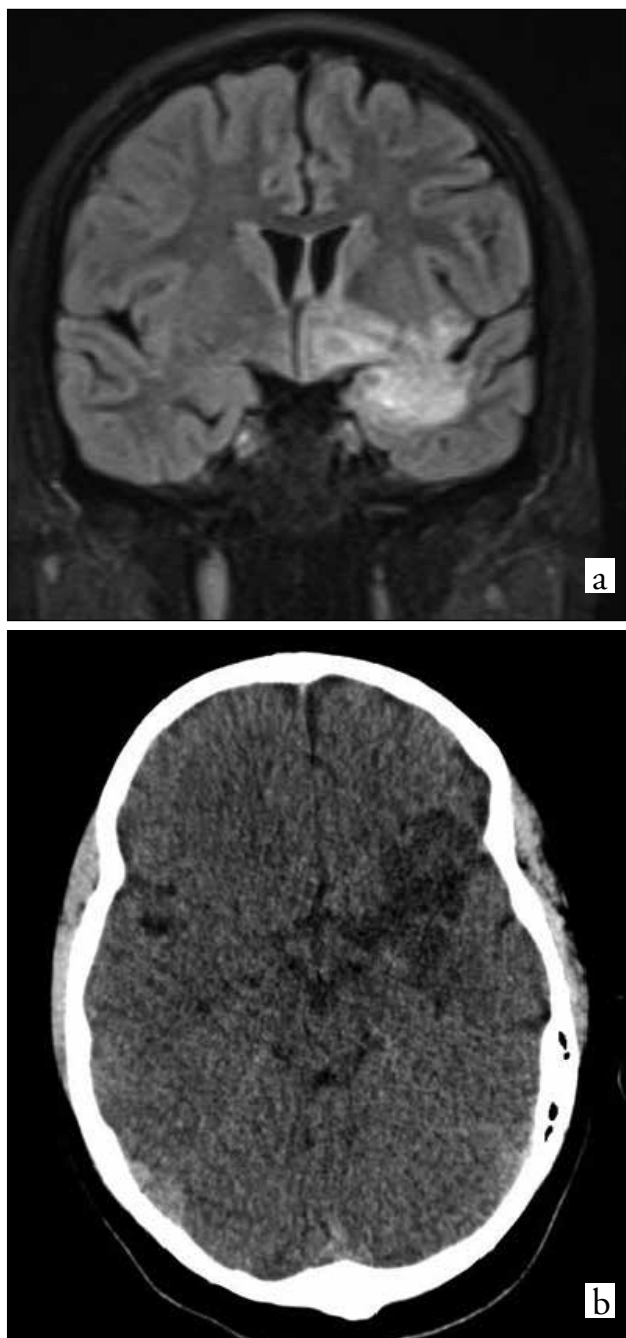


Figure 1. a, b. (a) In Flair images, an increased signal noted in the left insular cortex, left temporal lobe, hypothalamus, hippocampus and amygdala. (b) CT images demonstrate hypodensity in same locations

platelet count  $355.0 \mu\text{L}^{-1}$ , and sedimentation rate  $60 \text{ mm h}^{-1}$ , whereas C-reactive protein and procalcitonin were negative. A cranial magnetic resonance (MR) investigation that showed increased signal intensities and patchy contrast uptake in the anterior left temporal lobe, hypothalamic region, cerebral pedicle, hippocampus, amygdala and insula on the T2A and Flair sequences (Figure 1a, b). The MR angiography and venography were normal. Routine laboratory tests were also within the normal limits. A lumbar puncture was performed, which showed normal glucose, protein, and chloride levels

and the absence of any cellular elements in the cerebrospinal fluid (CSF). An abdominal ultrasonography was normal. An electroencephalography showed diffuse impairment of organisation, and deterioration with hyperventilation. Ceftriaxone and acyclovir treatments were started. On the 3<sup>rd</sup> day, her hemiparesis improved. Ceftriaxone was discontinued due to the absence of proliferation in the CSF culture. The herpes virus polymerase chain reaction was also negative in CSF. On the 15<sup>th</sup> day of follow-up, the facial paralysis persisted, and the patient now developed somnolence with deterioration of the clinical status within several hours. Informed consent was obtained from family, and the patient was transferred to the paediatric intensive care unit (PICU), where, having a Glasgow coma scale score of 8, she was intubated, connected to the mechanical ventilator and provided with respiratory support. She was also begun on midazolam and fentanyl infusions. As her blood pressure rose to 220/140 mmHg, esmolol  $500 \text{ mcg kg}^{-1}$  was loaded intravenously, followed by a maintenance infusion dose of  $50 \text{ mcg kg}^{-1} \text{ min}^{-1}$ . Since she remained hypertensive, the esmolol dose was gradually increased to  $200 \text{ mcg kg}^{-1} \text{ min}^{-1}$ . Oseltamivir and clarithromycin were added to acyclovir treatment. A repeat cranial MR examination with T1A and GE sequences revealed the areas of haemorrhagic necrosis containing haemorrhage products at the subacute stage in the medial part of temporal lobe and anterior thalamus (Figure 2a-c). Anti-TPO was  $112.3 \text{ IU mL}^{-1}$  (N:5-60), and Anti-Tg was  $74.6 \text{ IU mL}^{-1}$  (N:0-4). She was euthyroid. There was no oligoclonal band found in CSF. Autoimmune antibodies ruled out autoimmune encephalitis and were negative in CSF and serum. Antinuclear antibody, anti-double stranded DNA, anticardiolipin IgM and IgG, anti-topoisomerase I, anti-Smith antibody and Anti-Ro antibodies studied for other autoimmune disorders were negative. The CSF enterovirus was also negative. To rule out a paraneoplastic syndrome, an abdominal ultrasonography was performed, which revealed no pathology. Under the light of the available information, Hashimoto encephalitis was considered as the primary diagnosis. Methylprednisolone was administered at a dose of  $30 \text{ mg kg}^{-1}$  for 5 days, followed by prednisolone at a dose of  $1.5 \text{ mg kg}^{-1} \text{ day}^{-1}$ . As the patient's clinical status did not improve, a 11Fr haemodialysis catheter was placed, through which therapeutic plasma exchange (1/1 ratio) with fresh frozen plasma was applied for a total of 8 days, followed by IVIG  $1 \text{ gr kg}^{-1}$  for 2 days. Unfortunately, the patient did not respond to this treatment either. Therefore, rituximab and endoxane treatments were planned. However, the patient developed fever and increased pulmonary secretion. *S. pneumonia* proliferated in her tracheal aspirate culture. Teicoplanin was applied to treat ventilator-associated pneumonia, while rituximab and endoxane treatments were postponed. The patient developed septic shock on the 14<sup>th</sup> day following the PICU admission. Noradrenaline and dopamine were started with no response, and the patient died from sepsis.

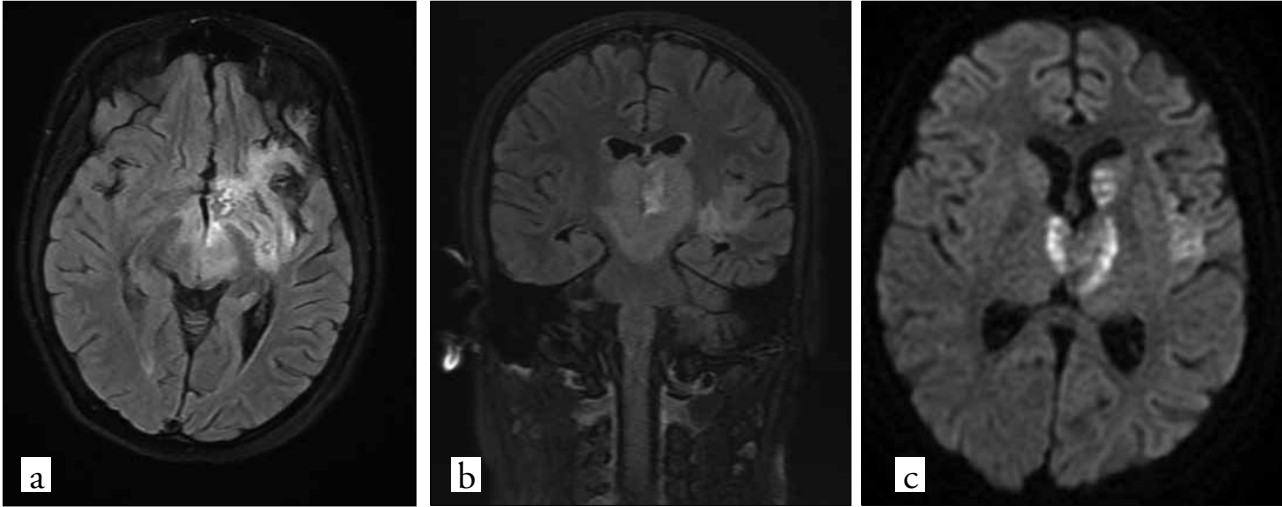


Figure 2. a-c. (a) After 1 month, the MR images demonstrate the progression of the disease. (b, c) Added increased T2 and Flair signal noted in the right thalamus and cerebellar peduncle with corresponding restriction diffusion

## Discussion

Hashimoto encephalopathy usually affects adults with a female-to-male ratio of 4:1. It is described as an autoimmune condition because it mostly affects women, has a fluctuated clinical course, is related to other autoimmune disorders, is associated with inflammatory CSF signs and shows a dramatic response to steroids (4). It is also known as steroid-responsive encephalopathy; HE is associated with autoimmune thyroiditis and characterised by elevated antithyroid antibody titres in the absence of encephalopathy, brain tumour, stroke, or infection (5).

Children generally become symptomatic with generalised tonic-clonic or complex partial seizures, hallucinations and confusion. Focal neurological signs are less common in children than adults (6). HE can be easily missed unless suspected. First, potential causes of encephalopathy such as infection, toxins, neoplasia, vasculitic syndromes, metabolic conditions and electrolyte disorders should be excluded. The main diagnostic criterion is antithyroid antibody positivity.

Former studies reported that 25%-30% of HE cases had subclinical hypothyroidism, 17%-30% had hypothyroidism, 7% had hyperthyroidism and 18%-45% were euthyroid (7). Computerised tomography and angiography are normal. Abnormal MRI findings may also be found, such as ischaemic lesions, demyelination, oedema and atrophy (8).

The first treatment option is an intravenous high-dose of methyl prednisolone ( $30 \text{ mg}^{-1} \text{ kg}^{-1} \text{ day}^{-1}$ ). In patients unresponsive to steroids or in the case of relapse, IVIG and plasmapheresis are the second line treatments. A correlation was found between lowering antithyroid antibody levels by plasma exchange and symptomatic improvement (9). Immunomodulators such as azathioprine, cyclophosphamide, methotrexate and mycophenolate mofetil are other treatment options. The normalisation of CSF, electroencephalogram and neuropsychological tests indicates the efficacy of

the treatment. Unfortunately, the rate of sequela is greater in children and adolescents (10).

## Conclusion

Hashimoto encephalopathy should be considered in the differential diagnosis of encephalopathy, when infectious, neoplastic, autoimmune, toxic and metabolic causes are excluded.

**Informed Consent:** Written informed consent was obtained from patients' parents who participated in this study.

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## References

1. Castillo P, Woodruff B, Caselli R, Vernino S, Lucchinetti C, Swanson J, et al. Steroid-responsive encephalopathy associated with autoimmune thyroiditis. *Arch Neurol* 2006; 63: 197-202. [\[CrossRef\]](#)
2. Graham BR, Shiff N, Nour M, Hasal S, Hunisman RR, Al-mubarak S. Hashimoto encephalopathy presenting with stroke-like episodes in an adolescent female: a case report and literature review. *Pediatr Neurol* 2016; 59: 62-70. [\[CrossRef\]](#)
3. Lee MJ, Lee HS, Hwang JS, Jung DE. A case of Hashimoto's encephalopathy presenting with seizures and psychosis. *Korean J Pediatr* 2012; 55: 111-3. [\[CrossRef\]](#)
4. Payer J, Petrovic T, Lisy L, Langer P. Hashimoto encephalopathy: A rare intricate syndrome. *Int J Endocrinol Metab* 2012; 10: 506-14. [\[CrossRef\]](#)
5. Bektaş O, Yılmaz A, Kendirli T, Siklar Z, Deda G. Hashimoto encephalopathy causing drug-resistant status epilepticus treated with plasmapheresis. *Pediatr Neurol* 2012; 46: 132-5. [\[CrossRef\]](#)
6. Kara B, Demirkol-Soysal D, Kabataş-Eryılmaz S, Karaböcüoğlu M, Darendeliler F, Çalışkan M. Hashimoto's encephalopathy in a ten-year-old girl. *Turk J Pediatr* 2007; 49: 215-7.
7. Ferracci F, Carnivale A. The neurological disorder associated with thyroid autoimmunity. *J Neurol* 2006; 8: 975-84. [\[CrossRef\]](#)
8. Chen N, Qin W, Wei C, Wang X, Li K. Time course of Hashimoto's encephalopathy revealed by MRI:report of two cases. *J Neurol Sci* 2011; 300: 169-72. [\[CrossRef\]](#)
9. Hussain NS, Rumbaugh J, Kerr D, Nath A, Hillis AE. Effects of prednisone and plasma exchange on cognitive impairment in Hashimoto encephalopathy. *Neurology* 2005; 64: 165-6. [\[CrossRef\]](#)
10. Erol I, Saygı S, Alehan F. Hashimoto's encephalopathy in children and adolescents. *Pediatr Neurol* 2011; 45: 420-2. [\[CrossRef\]](#)